Alzheimer's Disease And Inflammation: A Review Of Cellular And Therapeutic Mechanisms

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Abstract:

SUMMARY

1. Of the neurodegenerative diseases that cause dementia, Alzheimer's disease (AD) is the most common. Three major pathologies characterize the disease: senile plaques, neurofibrillary tangles and inflammation. We review the literature on events contributing to the inflammation and the treatments thought to target this pathology.

2. The senile plaques of AD consist primarily of complexes of the β-amyloid protein. This protein is central to the pathogenesis of the disease.

3. Inflammatory microglia are consistently associated with senile plaques in AD, although the classic inflammatory response (immunoglobulin and leucocyte infiltration) is absent. β-Amyloid fragments appear to mediate such inflammatory mechanisms by activating the complement pathway in a similar fashion to immunoglobulin.

4. Epidemiological studies have identified a reduced risk of AD in patients with arthritis and in leprosy patients treated with anti-inflammatory drugs. Longitudinal studies have shown that the consumption of anti-inflammatory medications reduces the risk of AD only in younger patients (< 75 years).

5. There is a considerable body of *in vitro* evidence indicating that the inflammatory response of microglial cells is reduced by non-steroidal anti-inflammatory drugs (NSAID). However, no published data are available concerning the effects of these medications on brain pathology in AD.

6. Cyclo-oxygenase 2 enzyme is constitutively expressed in neurons and is up-regulated in degenerative brain regions in AD. Non-steroidal anti-inflammatory drugs may reduce this expression.

7. Platelets are a source of β-amyloid and increased platelet activation and increased circulating β-amyloid have been identified in AD. Anti-platelet medication (including NSAID) would prevent such activation and its potentially harmful consequences.

8. Increased levels of luminal β-amyloid permeabilizes the blood-brain barrier (BBB) and increases vasoconstriction of arterial vessels, paralleling the alterations observed with infection and inflammation. Cerebral amyloidosis is highly prevalent in AD, compromising the BBB and vasoactivity. Anti-inflammatory medications may alleviate these problems.

Keywords: Alzheimer's disease; β-amyloid; anti- inflammatory medication; blood-brain barrier; inflammation; microglia; platelets; senile plaques

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